

December 5, 1955

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Dear Alan:

Thank you for the recalculations on bacterial radiography. One trouble is that we won't be able to make a specific correlation between  $P_{32}$  and gene segregation: i.e., at the 4-cell stage, only one cell will segregate out viable recombinants, but we can't tell which one. There are, however, any number of reasons why the experiment is worth doing. Conceivably, even at (say) the 32-cell stage, all the label will be in one cell: In that event, we can sample parts of the clones (or subclones) for their genotypes, and look for \*\*\* among any of those left. That is, for the most useful results, this experiment would be a refinement of Cy's.

What would you say to the idea of doing this together-- Would Seymour be likely to give you a few weeks off next summer or fall? You can tell him we'd pay the tab. By then, I hope to have the technique to be able to do my end of this kind of experiment, which I don't have now.

As to the diploids, we have never found  $Lp^+/Lp^+$  derivatives from  $Lp^+/Lp^s$  cells exposed to lambda. This is a puzzling result, but we want to do this with Gal-transduction as a tag. That's one reason I'm struggling to make some  $Lp^+/s$  Gal-/- diploids, but have had little luck so far. The other approach is to use some marked lambdas, and Esther has been hoping to set this up soon.

The growth of T4r on  $Lp^+/s$  may not be only a trivial experiment. Every diploid population is contaminated with 5-10% segregants, so one will have to do this on a statistical basis with single bursts, and guess whether the fraction of bursts corresponds to the  $Lp^s$  segregants or to the sum of these with  $Lp^+/s$  cells. With a good anti-T4 serum, it might not be too difficult to get a good count of infective centers, unless the heterozygotes show some unpredictable and confusing behavior. --- I think perhaps one could also take advantage of streptomycin resistance. Say we have a suspension with 85%  $Lp^+/s$ ; 10% s and 5% + segregants, which is not too unreasonable. The same diploid is segregating  $S^r/S^s$  so that most of the  $Lp^s$  and all of the +/s are sensitive to streptomycin; the  $Lp^s$  segregants are resistant. Infect with the T4, add serum to inactivate free phage, and plate for infective centers with and without sm. If the infective centers correspond to the T4-killed bacteria without sm, and to the T4-killed  $Lp^s$  with sm, then both +/s and s are growing T4. If the infective centers correspond only to the killed  $Lp^s$ , and are not reduced by sm, the only s grows the phage. I would not want to rely on a half-experiment without such a check. Is the result worth the trouble? The systems where lambda blocks killing by other phages give easier answers. But I'll be glad to try it if it seems important.

Sincerely.